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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,091	09/09/2003	David W. Old	17616 (AP)	2723

51957 7590 08/18/2006

ALLERGAN, INC., LEGAL DEPARTMENT
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EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,091	OLD ET AL.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *January 26, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This application was filed on September 9, 2003. Claims 1-22 are pending in this application and examined on the merits herein.

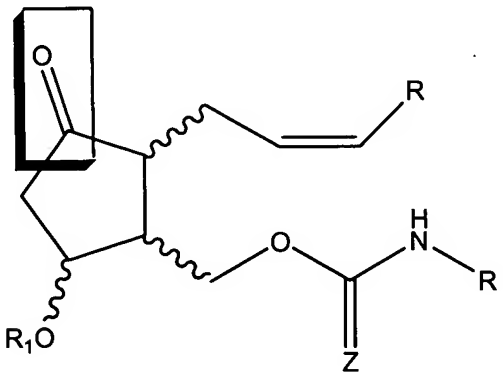
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

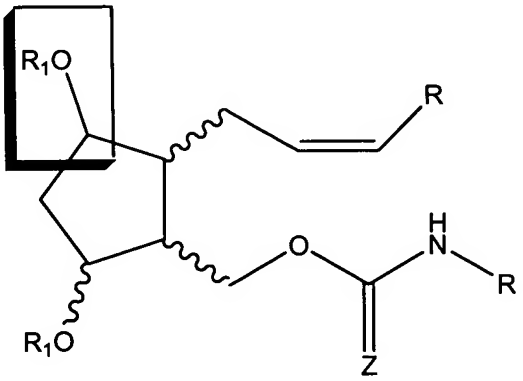
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 13-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burk (US patent 6291552, reference cited in PTO-892) in view of Bito. (US patent 4599353, Reference cited in PTO-892) Burk et al. discloses prostaglandin F_2 derivatives of a formula similar to that disclosed in instant claims 1, 9, 11, and 13, a method of using such compounds for treating ocular hypertension, and ophthalmic solutions containing such compounds. (column 3, lines 5-55) The only difference between the structures of Burk and those of the claimed invention is the identity of the functional group labeled U in the instant application, which is substituted with a hydroxyl or alkoxy in the structures of Burk. Burk et al. furthermore discloses additional structures similar to those described in instant claims 2, 10, 12, 14, and 15. Additionally, a number of specific embodiments are disclosed, including (Z)-7-((1R,2S,3R,5S)-2-benzylcarbamoyloxymethyl-3,5-dihydroxycyclopentyl)hept-5-enoic acid, (column 5, lines 1-2) which is similar to the species disclosed in instant claims 3-7 and 16-20. In every

case, the similar structures differ only by the occurrence of a hydroxyl or alkoxy group at position U instead of a ketone or halogen as claimed here. In other words, while the compounds described in the instant claims are derivatives of prostaglandin E_2, those disclosed by Burk are equivalent derivatives of prostaglandin F_2. The ophthalmic solutions disclosed by Burk are described in further detail from column 14, line 40 to column 15, line 47. Burk does not explicitly disclose the prostaglandin E_2 derivatives of the claimed invention, or therapeutic methods or ophthalmic solutions involving these compounds. The difference between the compounds of Burk and those of the claimed invention is illustrated below:



Compounds of the Claimed Invention



Compounds of Burk

Bito discloses a method of treating ocular hypertension comprising administering a prostaglandin to a subject suffering therefrom. (columns 3-12) In particular, prostaglandins E_2 and F_2 are disclosed to be effective in this therapeutic method when applied topically to the eyes as an ophthalmic solution.

It would have been obvious to one of ordinary skill in the art a the time of the invention to modify the invention of Burk by producing prostaglandin E_2 derivatives

similar to the prostaglandin F_2 derivatives disclosed by Burk, according to instant claims 13-22, and to formulate an ophthalmic solution comprising said compounds according to instant clams 9-10, and to use this solution in a method of treating ocular hypertension according to instant claims 1-8. One of ordinary skill in the art would have been motivated to make these modifications because, in view of Bito's disclosure that prostaglandins E_2 and F_2 are both useful in a method of treating ocular hypertension, derivatives of these two prostaglandins are also expected to function similarly and to be useful in the same compositions and methods. One of ordinary skill in the art would reasonably have expected success because the structures of the claimed invention are very similar to the structures of Burk, and are all PGE_2 analogs of PGF_2 derivatives included within the scope of structures disclosed by Burk.

Furthermore, as noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in

structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Thus the invention taken as a whole is *prima facie* obvious.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burk (US patent 6291552, reference cited in PTO-892) in view of Bito (US patent 4599353, Reference cited in PTO-892) further in view of Stand et al. (US patent 5152435, cited in PTO-892) Burk discloses prostaglandin F_2 derivatives of a formula similar to that disclosed in instant claim 13 and ophthalmic solutions containing such compounds. (column 3, lines 5-55) The similar structures differ only by the occurrence of a hydroxyl or alkoxy group at position U instead of a ketone or halogen as claimed here. In other words, while the compounds described in the instant claims are derivatives of prostaglandin E_2, those disclosed by Burk are equivalent derivatives of prostaglandin F_2. The ophthalmic solutions disclosed by Burk are described in further detail from column 14, line 40 to column 15, line 47. Burk does not explicitly disclose

the prostaglandin E_2 derivatives of the claimed invention, or a pharmaceutical product comprising a container adapted to dispense the contents of said container in metered form, and an ophthalmic solution in said container comprising one of these compounds.

Bito discloses a method of treating ocular hypertension comprising administering a prostaglandin to a subject suffering therefrom. (columns 3-12) In particular, prostaglandins E_2 and F_2 are disclosed to be effective in this therapeutic method when applied topically to the eyes as an ophthalmic solution.

Stand et al. discloses an ophthalmic dispensing pump for the administration of metered doses of ophthalmic solutions to the eye. (column 3, lines 35-46) This device is a container adapted to dispense the contents of said container in metered form, according to instant claim 11.

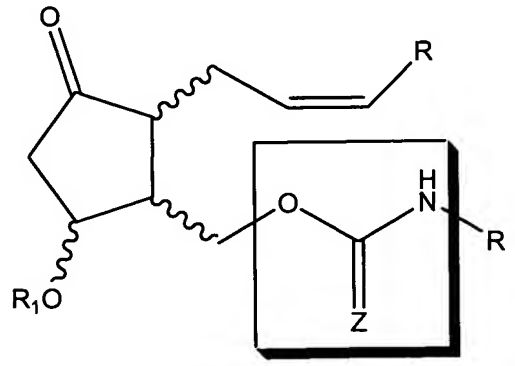
It would have been obvious to one of ordinary skill in the art a the time of the invention to modify the invention of Burk by producing prostaglandin E_2 derivatives similar to the prostaglandin F_2 derivatives disclosed by Burk, to formulate an ophthalmic solution comprising said compounds, and to dispense this ophthalmic solution in a container according to Stand et al., in order to practice the invention of instant claims 11-12. One of ordinary skill in the art would have been motivated to make these modifications because, in view of Bito's disclosure that prostaglandins E_2 and F_2 are both useful in a method of treating ocular hypertension, derivatives of these two prostaglandins are also expected to function similarly and to be useful in the same compositions and methods. One of ordinary skill in the art would have been motivated to dispense the solution in a container comprising a pump according to Stand et al.

because Stand et al. discloses that their pump is intended for this purpose. (i.e. dispensing metered doses of an ophthalmic solution) One of ordinary skill in the art would reasonably have expected success because the structures of the claimed invention are very similar to the structures of Burk, and are all PGE_2 analogs of PGF_2 derivatives included within the scope of structures disclosed by Burk. Furthermore, the patient pack or container adapted to dispense an ophthalmic solution is deemed obvious since it is well within the knowledge and conventional skills of a pharmacologist to assist the user and prescriber for easy dispensing of the medication.

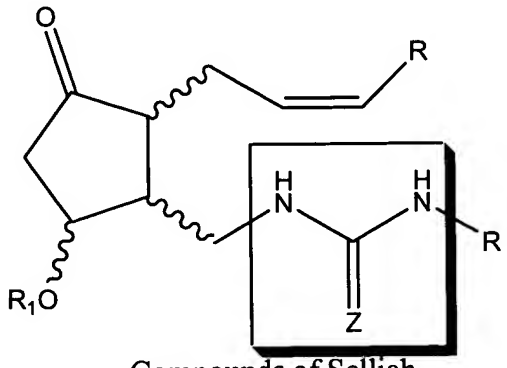
Thus the invention taken as a whole is *prima facie* obvious.

Claims 1-8 and 13-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selliah (US patent 6160013, reference cited in PTO-892) in view of Silverman. (Reference included with PTO-892) Selliah discloses a number of derivatives of prostaglandins D_2, E_2, and F_2. (column 4, line 49 – column 5, line 56, particularly structure I) Embodiments of this structure include those in which R^{2A} and R^{2B} together for m a ketone, and one of R^{3A} and R^{3B} is hydroxyl or alkoxy and the other is hydrogen, and thus the cyclopentyl ring is identical to the equivalent ring in the structures disclosed in instant claims 1, 9, 11, and 13. (formula I found in column 4, lines 49-62) Further embodiments of this formula include those in which X = NH, Y = CH_2 or a direct bond, Z^2 = alkyl or aryl, and G = CH_2. (column 4, line 62 – column 5, line 56) These embodiments are similar to compounds included within the scope of the compounds of instant claims 13-15 in which U represents a ketone and include within their scope

compounds similar to the compounds of instant claims 16-22. The only difference between the compounds of instant clams 13-22 and these embodiments of the compounds of Selliah is that the compounds of Selliah et al. include a urea substructure in place of the carbamoyl substructure of the compounds of the claimed invention. Selliah also discloses that these compounds may be formulated into various pharmaceutical compositions, preferably an aqueous solution, suspension, or emulsion for topical administration to a patient's eyes, similar to the solutions of instant claims 9-10. (column 15, lines 1-18) Selliah also discloses that these compounds and ophthalmic solutions are useful in a method of treating glaucoma and ocular hypertension similar to those described in instant claims 1-8. (column 4, lines 12-48) Selliah further discloses that the naturally-occurring prostaglandins, including PGE_2, possess ocular hypotensive activity as well. (column 2, lines 8-40) Selliah does not disclose compounds containing a carbamoyl group in the same position as the structures of the instant claims, (i.e. one in which the nitrogen closest to the cyclopentyl ring is changed into an oxygen) or compositions and methods involving such compounds. The difference between the compounds of Selliah and those of the claimed invention is illustrated below:



Compounds of the Claimed Invention



Compounds of Selliah

Silverman discloses that certain functional groups, known as bioisosteres, may be substituted for one another while conserving the overall biological activity of a compound. (p. 19, second paragraph) –CONHR and –COOR functionalities are disclosed as bioisosteres. (p. 19, table 2.2, line 2b) Therefore, carbamoyl/thiocarbamoyl and urea/thiourea groups are expected to be functionally equivalent in pharmaceutical agents. This is especially the case in this instance because the conjugation of the nitrogen to the adjacent carbonyl is expected to attenuate its Bronstead and Lewis base properties.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Selliah by substituting an oxygen for a nitrogen in the indicated position, thus producing the compounds, ophthalmic solutions, and therapeutic methods of the claimed invention. One of ordinary skill in the art would have been motivated to make this modification because Silverman discloses that this transformation between two bioisosteric compounds is expected to preserve the biological activity of the parent compound. One of ordinary skill in the art would reasonably have expected success because the claimed compounds are structurally and chemically very similar, and furthermore because the parent compound prostaglandin E_2, which also possesses ocular hypotensive activity, has a methylene at this position, indicating that the nitrogen is not essential for the biological activity of the compounds.

As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the

claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Thus the invention taken as a whole is *prima facie* obvious.

Claims 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selliah (US patent 6160013, reference cited in PTO-892) in view of Silverman (Reference included with PTO-892) further in view of Stand et al. (US patent 5152435,

cited in PTO-892) The disclosure of Selliah is as discussed in the rejection made above under 35 USC 103. Selliah does not disclose the prostaglandin E_2 derivatives of the claimed invention, or a pharmaceutical product comprising an ophthalmic solution comprising a container adapted to dispense the contents of said container in metered form, and an ophthalmic solution in said container comprising one of these compounds..

Silverman discloses that certain functional groups, known as bioisosteres, may be substituted for one another while conserving the overall biological activity of a compound. (p. 19, second paragraph) –CONHR and –COOR functionalities are disclosed as bioisosteres. (p. 19, table 2.2, line 2b) Therefore, carbamoyl/thiocarbamoyl and urea/thiourea groups are expected to be functionally equivalent in pharmaceutical agents. This is especially the case in this instance because the conjugation of the nitrogen to the adjacent carbonyl is expected to attenuate its Bronstead and Lewis base properties.

Stand et al. discloses an ophthalmic dispensing pump for the administration of metered doses of ophthalmic solutions to the eye. (column 3, lines 35-46) This device is a container adapted to dispense the contents of said container in metered form, according to instant claim 11.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the invention of Selliah by substituting an oxygen for a nitrogen in the indicated position, thus producing the compounds, ophthalmic solutions, and therapeutic methods of the claimed invention, and to dispense the ophthalmic solution in the pump disclosed by Stand et al. One of ordinary skill in the art would have been

motivated to make this modification because Silverman discloses that this transformation between two bioisosteric compounds is expected to preserve the biological activity of the parent compound. One of ordinary skill in the art would have been motivated to dispense the solution in a container comprising a pump according to Stand et al. because Stand et al. discloses that this pump is intended for this purpose. (i.e. dispensing metered doses of an ophthalmic solution) One of ordinary skill in the art would reasonably have expected success because the claimed compounds are structurally and chemically very similar, and furthermore because the parent compound prostaglandin E_2, which also possesses ocular hypotensive activity, has a methylene at this position, indicating that the nitrogen is not essential for the biological activity of the compounds. Furthermore, the patient pack or container adapted to dispense an ophthalmic solution is deemed obvious since it is well within the knowledge and conventional skills of a pharmacologist to assist the user and prescriber for easy dispensing of the medication.

Thus the invention taken as a whole is *prima facie* obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir.

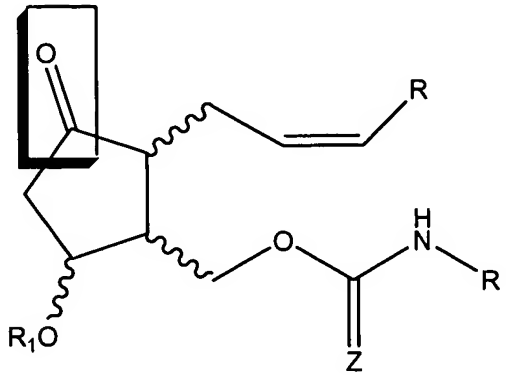
1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

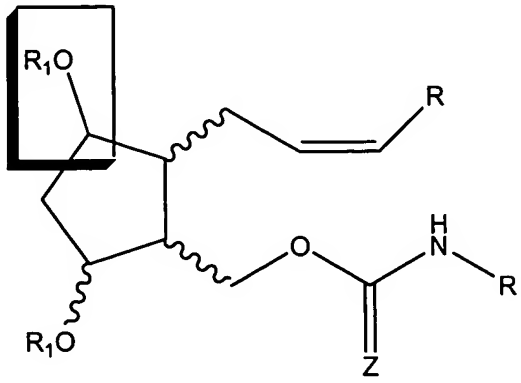
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 and 13-22 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6291522 (Reference cited in PTO-892, herein referred to as Burk) in view of US patent 4599353. (Reference cited in PTO-892, herein referred to as Bito) Claims 8-12 of Burk et al. disclose prostaglandin F_2 derivatives of a formula similar to that disclosed in instant claims 1-2 and 9-15. Claims 1-6 of Burk disclose a method of using such compounds for treating ocular hypertension. The only difference between the structures of Burk and those of the claimed invention is the identity of the functional group labeled U in the instant application, which is substituted with a hydroxyl or alkoxy in the structures of Burk. Additionally, a number of specific embodiments are disclosed in claims 7 and 15 of Burk, including (Z)-7-((1R,2S,3R,5S)-2-benzylcarbamoyloxymethyl-3,5-dihydroxycyclopentyl)hept-5-enoic acid, which is similar to the species disclosed in instant claims 3-7 and 16-20. In every case, the similar structures differ only by the occurrence of a hydroxyl or alkoxy group at position U instead of a ketone or halogen. In other words, while the compounds described in the instant claims are derivatives of prostaglandin E_2, those disclosed by Burk are equivalent derivatives of prostaglandin F_2.

Claims 1-13 of Burk do not explicitly disclose the prostaglandin E_2 derivatives of the claimed invention, or therapeutic methods or ophthalmic solutions involving these compounds. The difference between the compounds of Burk and those of the claimed invention is illustrated below:



Compounds of the Claimed Invention



Compounds of Burk

Burk also does not explicitly disclose an ophthalmic solution as described by instant claims 9-10.

Bito discloses a method of treating ocular hypertension comprising administering a prostaglandin to a subject suffering therefrom. (columns 3-12) In particular, prostaglandins E_2 and F_2 are disclosed to be effective in this therapeutic method when applied topically to the eyes as an ophthalmic solution.

It would have been obvious to one of ordinary skill in the art a the time of the invention to modify the invention of Burk by producing prostaglandin E_2 derivatives similar to the prostaglandin F_2 derivatives disclosed by Burk, according to instant claims 13-22, to formulate an ophthalmic solution comprising said compounds according to instant clams 9-10, and to use this solution in a method of treating ocular hypertension

according to instant claims 1-8. One of ordinary skill in the art would have been motivated to make these modifications because, in view of Bito's disclosure that prostaglandins E_2 and F_2 are both useful in a method of treating ocular hypertension, derivatives of these two prostaglandins are also expected to function similarly and to be useful in the same compositions and methods. One of ordinary skill in the art would have been motivated to prepare an ophthalmic solution comprising the compounds disclosed by claims 8-13 of Burk because the method of claim 1 of Burk involves administering these compounds to treat ocular hypertension, thereby implying that they be formulated into a suitable ophthalmic dosage form. One of ordinary skill in the art would reasonably have expected success because the structures of the claimed invention are very similar to the structures of Burk, and are all PGE_2 analogs of PGF_2 derivatives included within the scope of structures disclosed by Burk.

As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be

presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Thus the invention taken as a whole is *prima facie* obvious.

Claims 9-12 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6291522 (Reference cited in PTO-892, herein referred to as Burk) in view of US patent 4599353. (Reference cited in PTO-892, herein referred to as Bito) further in view of US patent 5152435 (cited in PTO-892, herein referred to as Stand et al.) Claims 8-12 of Burk et al. disclose prostaglandin F_2 derivatives of a formula similar to that disclosed in instant claims 1-2 and 9-15. Claims 1-6 of Burk disclose a method of using such compounds for treating ocular hypertension. The only difference between the structures of Burk and those of the claimed invention is the identity of the functional group labeled U in the instant application, which is substituted with a hydroxyl or alkoxy in the structures of Burk. Additionally, a number of specific embodiments are disclosed in claims 7 and 15

of Burk, including (Z)-7-((1R,2S,3R,5S)-2-benzylcarbamoyloxymethyl-3,5-dihydroxycyclopentyl)hept-5-enoic acid, which is similar to the species disclosed in instant claims 3-7 and 16-20. In every case, the similar structures differ only by the occurrence of a hydroxyl or alkoxy group at position U instead of a ketone or halogen. In other words, while the compounds described in the instant claims are derivatives of prostaglandin E_2, those disclosed by Burk are equivalent derivatives of prostaglandin F_2. Claims 1-13 of Burk do not explicitly disclose the prostaglandin E_2 derivatives of the claimed invention, or a pharmaceutical product comprising a container adapted to dispense the contents of said container in metered form, and an ophthalmic solution in said container comprising one of these compounds.

Bito discloses a method of treating ocular hypertension comprising administering a prostaglandin to a subject suffering therefrom. (columns 3-12) In particular, prostaglandins E_2 and F_2 are disclosed to be effective in this therapeutic method when applied topically to the eyes as an ophthalmic solution.

Stand et al. discloses an ophthalmic dispensing pump for the administration of metered doses of ophthalmic solutions to the eye. (column 3, lines 35-46) This device is a container adapted to dispense the contents of said container in metered form, according to instant claim 11.

It would have been obvious to one of ordinary skill in the art a the time of the invention to modify the invention of Burk by producing prostaglandin E_2 derivatives similar to the prostaglandin F_2 derivatives disclosed by Burk, to formulate an ophthalmic solution comprising said compounds, and to dispense this ophthalmic solution in a

container according to Stand et al., in order to practice the invention of instant claims 11-12. One of ordinary skill in the art would have been motivated to make these modifications because, in view of Bito's disclosure that prostaglandins E_2 and F_2 are both useful in a method of treating ocular hypertension, derivatives of these two prostaglandins are also expected to function similarly and to be useful in the same compositions and methods. One of ordinary skill in the art would have been motivated to prepare an ophthalmic solution comprising the compounds disclosed by claims 8-13 of Burk because the method of claim 1 of Burk involves administering these compounds to treat ocular hypertension, thereby implying that they be formulated into a suitable ophthalmic dosage form. One of ordinary skill in the art would have been motivated to dispense the solution in a container comprising a pump according to Stand et al. because Stand et al. discloses that their pump is intended for this purpose. (i.e. dispensing metered doses of an ophthalmic solution) One of ordinary skill in the art would reasonably have expected success because the structures of the claimed invention are very similar to the structures of Burk, and are all PGE_2 analogs of PGF_2 derivatives included within the scope of structures disclosed by Burk. Furthermore, the patient pack or container adapted to dispense an ophthalmic solution is deemed obvious since it is well within the knowledge and conventional skills of a pharmacologist to assist the user and prescriber for easy dispensing of the medication.

Thus the invention taken as a whole is *prima facie* obvious.

Conclusion

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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